REMARKS

Claims 7-39 and 43-48 are pending in the present application. By this Amendment, Claims 40-42 have been cancelled, Claims 45-48 have been added, Claims 7-12, 16, 18-20, 22, 24-28, and 44 have been amended. Support for the new claims and amendments is found in Claim 20, Figures 1-5, and throughout the specification, especially pages 14-17. No new matter has been added by these amendments.

The Specification and Claims 7-8, 26 and 27 were amended to correct typographical errors. One skilled in the art would immediately recognize that the typographical errors that appear on page 14, line 5, and continuing to page 15, line 10, and in Claims 7-8, 26 and 27, would result in situations where nitrogen would have 4 bonds, carbon would have 5 bonds, and the oxygen of the carboxyl group would have a single bond as indicated in the Figures and in the specification. Those skilled in the art would readily recognize that nitrogen has 3 bonds, carbon has 4 bonds, and the oxygen of the carboxyl group has a double bond as indicated in the Figures and in the specification. The Applicant did not intend for the structures to show nitrogen with 4 bonds, carbon with 5 bonds or a carboxyl group with a single bond oxygen as demonstrated in Figures 1-5. Claims 26 and 27 were amended to expand the definition of R_6 as shown on page 17, lines 1-4, of the specification. In addition, Claims 7-12, 18-20, 22, 24-28, 44 were amended to recite alternatives in a format as exemplified in MPEP 2173.05(h). Applicant asserts such amendment does not reduce the scope of the respective claims. Applicants respectfully request reconsideration of the present claims in view of the foregoing amendments and the following remarks.

I. Formal Matters

Rejection of Claim 8 Under 35 U.S.C. § 112

Claim 8 is rejected under 35 U.S.C. § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter for "improper claim dependency onto itself". Applicant respectfully submits that the rejection has been obviated in view of the foregoing amendment and requests withdrawal of the rejection.

II. Allowable Subject Matter

Applicant appreciates the Examiner's indication that Claims 7-44 are free of the prior art of record. Applicant respectfully submits that the amendments do not admit new matter and the claims remain free of the prior art of record.

III. Telephone Interview with Examiner Jones

Applicant thanks the Examiner for granting a telephone interview on November 14, 2001 at 2:00 p.m. to discuss two references from the Information Disclosure Statement filed January 14, 2000 and to clarify whether an earlier restriction was waived. Applicant's representatives, Jeffery Arnold and Cheryl Huseman participated.

Examiner Jones stated that the previous restriction was waived and that all species were brought back into the invention once the prior art references were overcome by the Response of June 4, 2001.

Examiner Jones agreed that the references *Treatment of Refractory Rheumatoid Arthritis – The Thalidomide Experience* by Gutierrez-Rodriguez (HE on the IDS filed January 14, 2000), and WO 95/04533 to Andrulis (AT on the IDS filed January 14, 2000), disclose the treatment of Rheumatoid Arthritis (RA) with thalidomide and NSAIDS. The Examiner agreed that a claim amendment adding a negative proviso to eliminate thalidomide would make Claims 7, 26, and 27 allowable over these references. Examiner Jones also agreed that a new claim drawn to thalidomide and NSAIDS for treatment of angiogenic associated diseases other than RA would be appropriate if the applicant chose to submit one.

Applicant's representatives stated that amendments to the specification and claims were necessary to correct typographical errors and pointed out the location of the errors on pages 14 and 16 of the specification as filed. All parties discussed and agreed that one skilled in the art would recognize that these were inadvertent errors that, in certain situations, would result in an improper number of bonds for the elements carbon and nitrogen in the composition. Correction would not add new matter.

Applicant is very appreciative of the Examiner's time and help on these matters.

IV. Conclusion

Applicants respectfully submit that Claims 7-39 and 43-44 are now in condition for allowance and accordingly request allowance of the application.

Should the Examiner believe that anything further is necessary to place the application in better condition for allowance, the Examiner is respectfully requested to contact Applicant's representative at the telephone number listed below.

No fees are believed due, however, the Commissioner is hereby authorized to charge any additional fees, which may be required, or credit any overpayment to Deposit Account No.11-0855.

Respectfully submitted,

Respectfully submitted,

Cheryl L. Huseman

By: Cheryl L. Huseman
Reg. No. 45,392

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KS File #: 42615-213970
Our Docket: 03757-0272

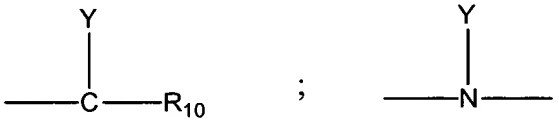
Version With Markings To Show Changes Made Under 37 C.F.R. § 1.121(C)(1)(Ii)

Please amend the written description and the claims by deleting the bracketed word(s) and inserting the underlined word(s) as indicated.

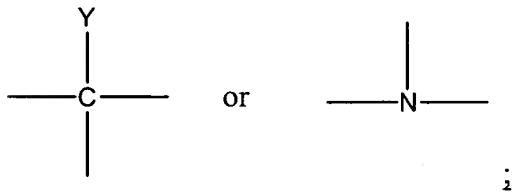
In the Specification:

Please amend the paragraph starting on page 14, line 5 and continuing to page 15, line 10 as follows:

-- In the above formulae, A), B), and C), R_1, R_2, R_3 and R_4 can be selected from: -H; -OH; =O, straight and branched chain alkanes, alkenes, alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acids, esters, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; $-XO_n$ or $-O-XO_n$, where X=N and n=2; X=S and n=2 or 3; or X=P and n=l-3; and halogens; R_5, R_6, and R_7[, and R8] are each independently selected from:



or -O- where Y is optional and is the same as defined above for R_1; and R_{10} is the same as defined above for R_1, or when Y is absent, R_{10} is =O; where R_8 is independently selected from:



;

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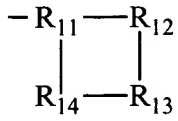
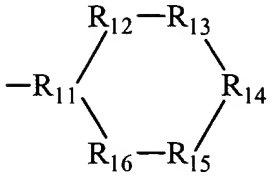
and R_9 is a moiety having formula D), E), F), G) or H):

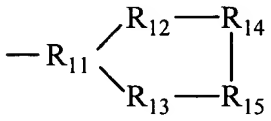
D)



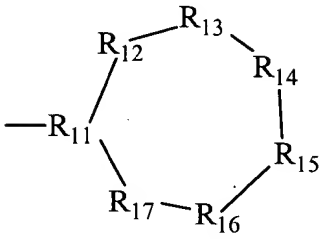
F)



E)

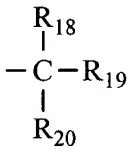


G)

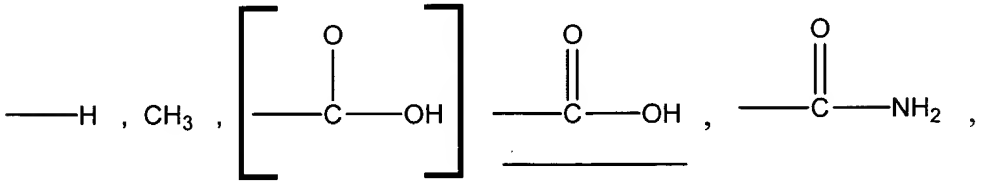


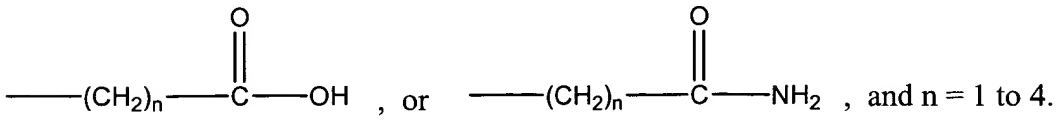
where each of $[R_{11}]R_{12}$ - R_{17} is independently the same as defined above for R_5; where R_{11} is independently the same as defined above for R_8;

H)



where R_{18}, R_{19} and R_{20} are[,] independently selected from





and n = 1 to 4.

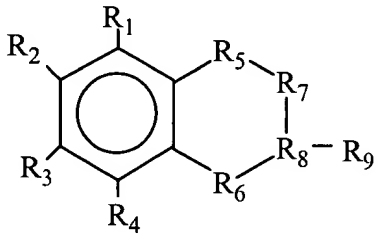
In the Claims:

--7. (Twice amended) An angiogenesis inhibitory composition comprising an angiogenesis inhibiting compound and an anti-inflammatory drug,

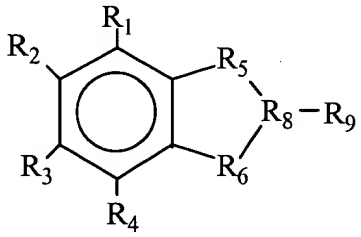
wherein the angiogenesis inhibiting compound is selected from [the group consisting of]:

(1) a compound selected from the formula

A)

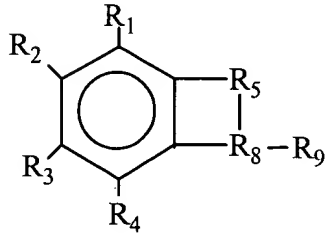


B)



or

C)

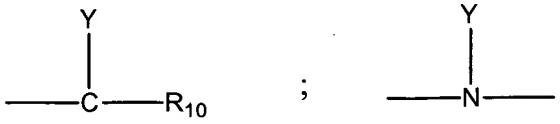


wherein

R_1 - R_4 are each independently selected from ±H; ±OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol,

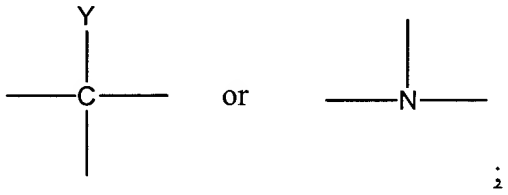
aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; $-XO_n$ or $-O-XO_n$, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens;

$R_5 - [R_8]R_7$ are each independently selected from



or -O-, where Y is absent and R_{10} is =O or Y and R_{10} are each independently the same as R_1;

where R_8 is independently selected from:



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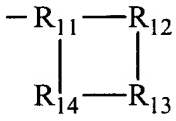
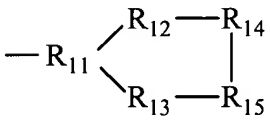
and R_9 is a moiety selected from [the group consisting of]

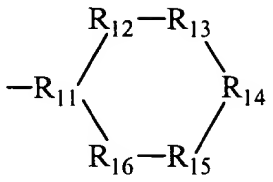
D)



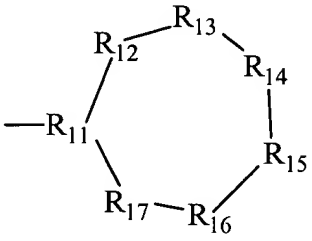
E)



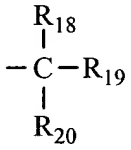
F)



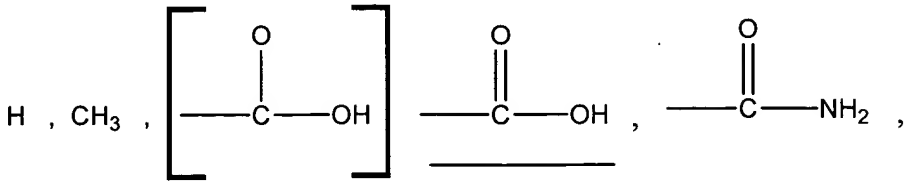
G)

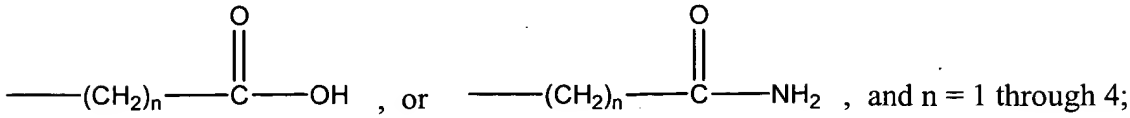


[and]or H)



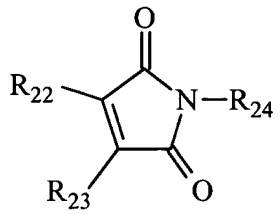
wherein each of [R_{11}] R_{12} - R_{17} is independently the same as R_5, wherein R_{11} is independently the same as R_8; and wherein R_{18}, R_{19} and R_{20} are each independently selected from





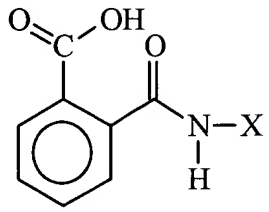
with the proviso that the angiogenesis inhibitory compound is not thalidomide;

(2) a compound selected from the formula

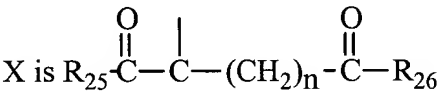


where R_{22} and R_{23} are each independently H, F, C_l, Br, I, CH_3, or $-CH_2-CH_3$;
and R_{24} is H, CH_3, or $-CH_2-CH_3$;
and

(3) a compound selected from the formula



where X is R_6 as defined in (1) above or



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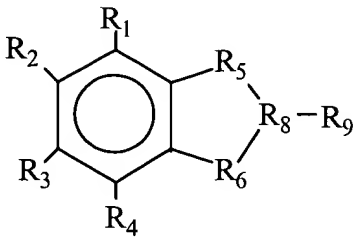
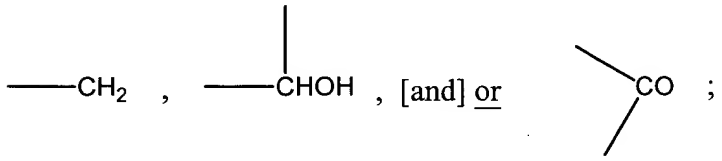
and R_{25} and R_{26} are independently -OH, -H, or $-NH_2$, and n=1 through 4.--

--8. (Amended) The angiogenesis inhibitory composition of Claim 7 wherein the angiogenesis inhibiting compound has the formula

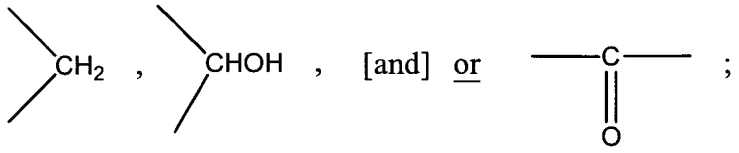
B)



wherein R_1-R_4 are as defined in Claim [8]7;
R_5 and R_6 are independently selected from [the group consisting of]



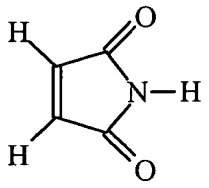
and R_9 is selected from F) or H) wherein R_{14} and R_{16} are each independently selected from [the group consisting of]



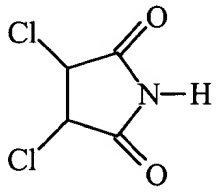
and R_{15} is -O- or $-\overset{R_{21}}{\underset{|}{N}}-$, where R_{21} is H, CH_3, or OH. --

--9. (Amended) The angiogenesis inhibitory composition of claim 7 wherein the angiogenesis inhibiting compound is selected from [the group consisting of]

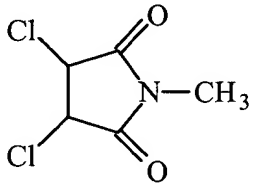
I)



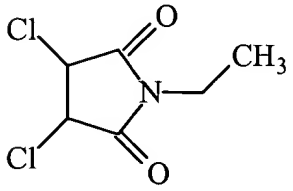
J)



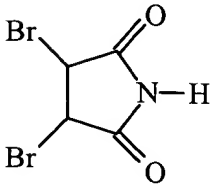
K)



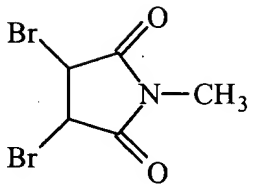
L)



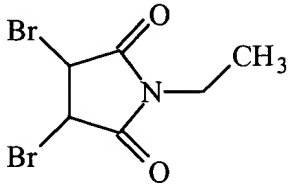
M)



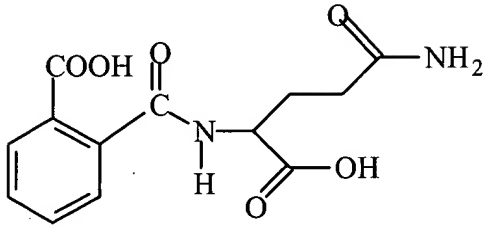
N)



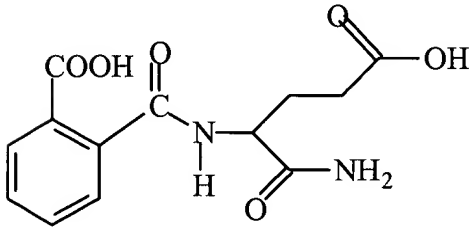
O)



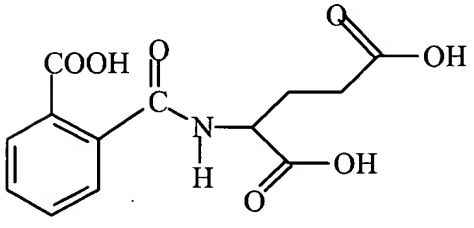
P)



Q)

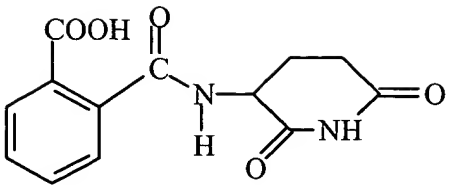


R)



[and]or

S)

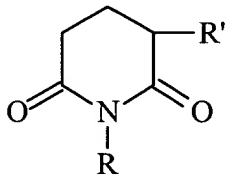


.--

--10. (Amended) The angiogenesis inhibitory composition of Claim 7 wherein the angiogenesis inhibiting compound is selected from [the group consisting of] [thalidomide,] metabolites of thalidomide, thalidomide analogs, epoxides of thalidomide, [hydolysis]hydrolysis products thereof, hydrolysis products of thalidomide, EM-12, metabolites of EM-12, epoxides of EM-12, [hydolysis]hydrolysis products thereof, EM-138, metabolites of EM-138, epoxides of EM-138, [hydolysis]hydrolysis products thereof, N-phthaloyl-DL-glutamic acid (PGA), N-phthaloyl-DL-glutamine anhydride, [and]or mixture thereof.--

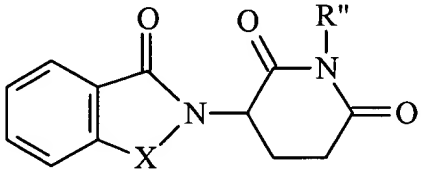
--11. (Amended) The angiogenesis inhibitory composition of Claim 10 wherein the angiogenesis inhibiting compound is selected from

(I)



[and]or

(II)

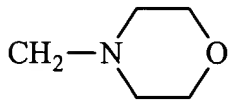


wherein
R is selected from [the group consisting of] H, (C_1-C_6)alkyl, phenyl, [and]or benzyl; and

R' is selected from [the group consisting of] phthalimido [and]or succinimido;

wherein
X is CH_2 or C=O; and

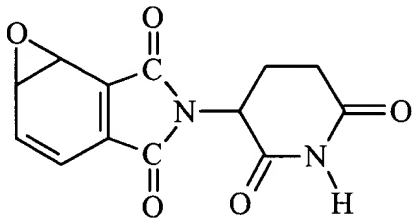
R" is H, $-CH_2CH_3$, $-C_6H_5$, $-CH_2C_6H_5$, $-CH_2CH=CH_2$, or



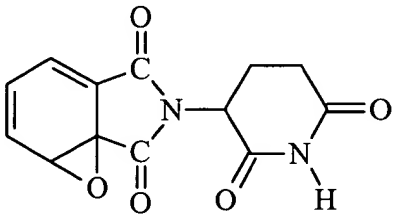
[and]or
(III) hydrolysis products of (II) wherein R" is H and the piperidino ring or both the piperidino and the imido ring are hydrolyzed.--

--12. (Amended) The angiogenesis inhibitory composition of Claim 10 wherein the angiogenesis inhibiting compound is selected from [the group consisting of]

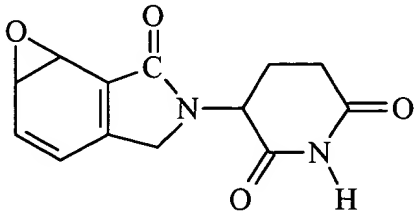
III)



IV)



V)



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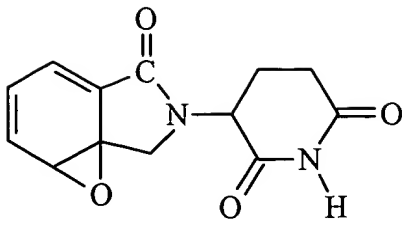
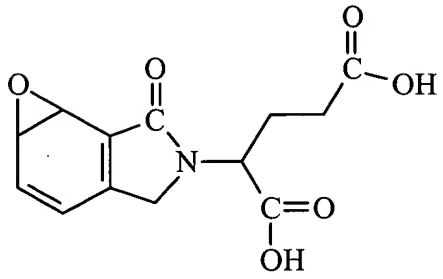


VII)



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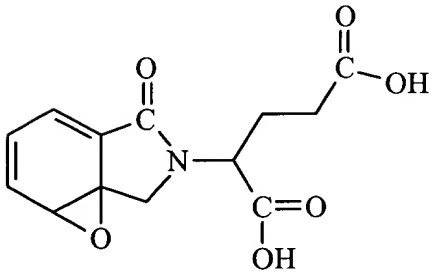

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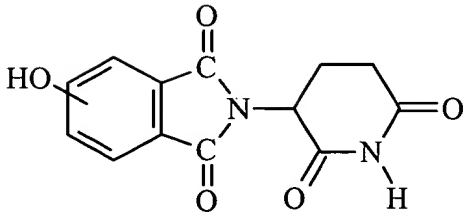
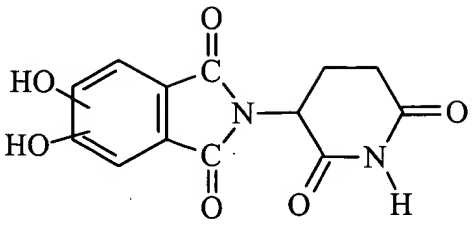
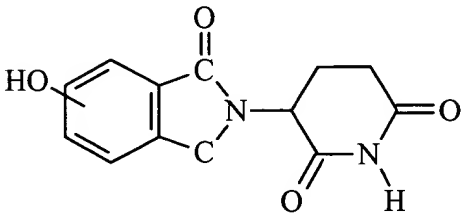


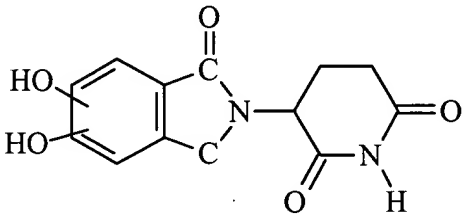
X)



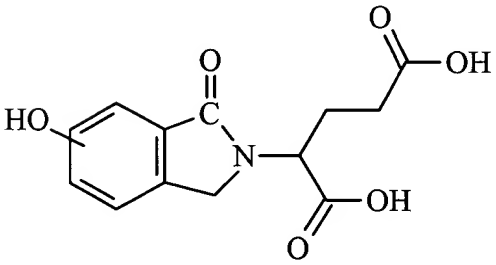
XI)



XII)

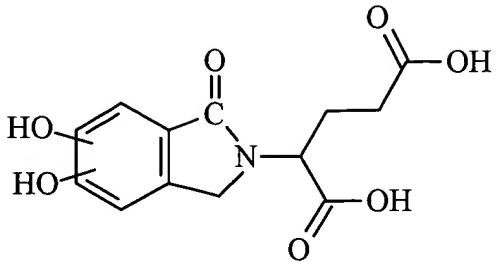


XIII)



[and]<u>or</u>

XIV)



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--16. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising a nonsteroidal, anti-inflammatory drug (NSAID) with the proviso that the angiogenesis dependent disease is not rheumatoid arthritis.--

--18. (Amended) The method of Claim 16 wherein the angiogenesis dependent disease is macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phylectenulosis, syphilis, *Mycobacteria* infections, lipid degeneration , chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, [rheumatoid arthritis,] systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications,[and]or rubeosis.--

--19. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, with the proviso that the angiogenesis inhibiting compound is not thalidomide.--

--20. (Amended) The method of Claim 19 wherein the angiogenesis dependent disease is selected from [the group consisting of] macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasia, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phylectenulosis, syphilis, *Mycobacteria* infections, lipid degeneration , chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis, systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, [and]or rubeosis.--

--22. (Amended) The angiogenesis inhibitory composition of Claim 21 wherein the steroid is selected from [the group consisting of] cortisol, corticosterone, hydrocortisone, hydrocortisol, cortisone, prednisone, prednisolone, dexamethasone, beclomethasone, betamethasone, mometasone, mometasone furoate, budesonide, triamcinolone acetonide, [and]or fluticasone.--

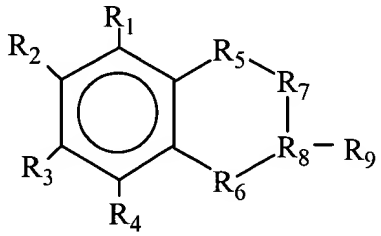
--24. (Amended) The angiogenesis inhibitory composition of Claim 23 wherein the NSAID is selected from aspirin, acetominophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (a cyclooxygenase-2 inhibitor), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, floctafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, [and]or tenoxicam.--

--25. (Amended) The angiogenesis inhibitory composition of Claim 23 wherein the NSAID is selected from indomethacin [and]or sulindac.--

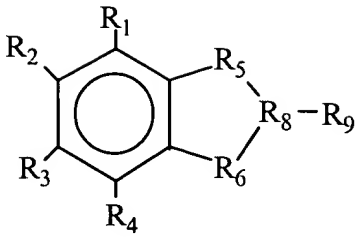
--26. (Amended) A method for inhibiting angiogenesis in a human or animal comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an anti-inflammatory compound, wherein the angiogenesis inhibiting compound is selected from [the group consisting of]:

(1) a compound selected from the formula

A)

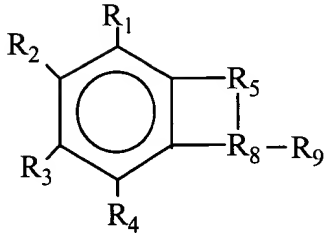


B)



or

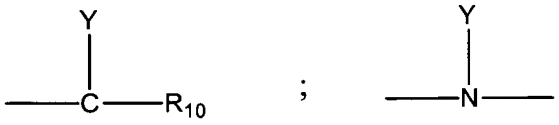
C)



wherein

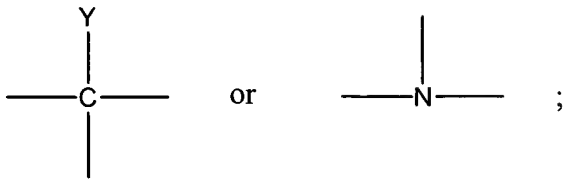
R_1 - R_4 are each independently selected from ±H; ±OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; $-XO_n$ or $-O-XO_n$, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens;

$R_5 - [R_8]R_7$ are each independently selected from



or -O-, where Y is absent and R_{10} is =O or Y and R_{10} are each independently the same as R_1;

where R_8 is independently selected from:



;

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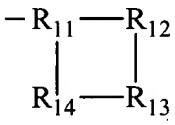
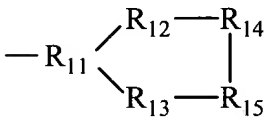
and R_9 is a moiety selected from [the group consisting of]

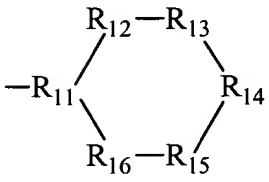
D)



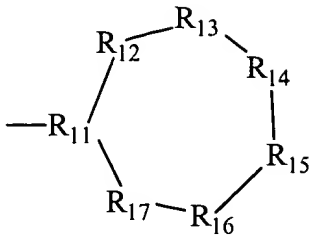
E)



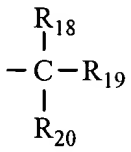
F)



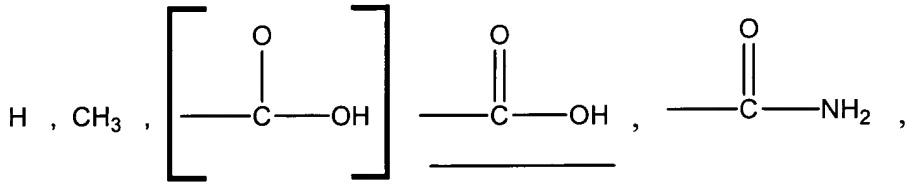
G)

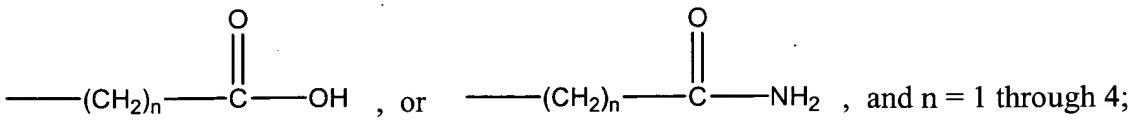


[and]or H)



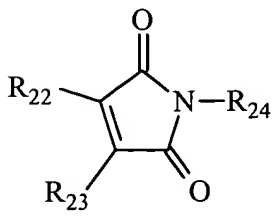
wherein each of [R_{11}] R_{12} - R_{17} is independently the same as R_5, wherein R_{11} is independently the same as R_8; and wherein R_{18}, R_{19} and R_{20} are each independently selected from





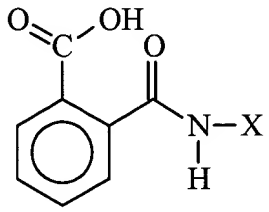
with the proviso that the angiogenesis inhibiting compound is not thalidomide;

(2) a compound selected from the formula

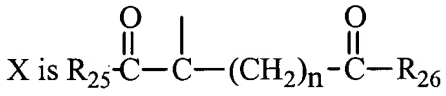


where R_{22} and R_{23} are each independently H, F, C_l, Br, I, CH_3, or $-CH_2-CH_3$;
and R_{24} is H, CH_3, or $-CH_2-CH_3$;
and

(3) a compound selected from the formula



where X is R_6 as defined in (1) above or



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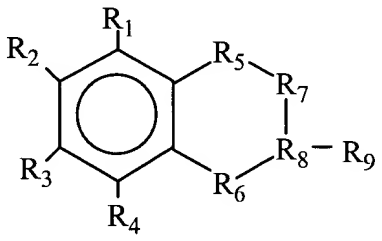
and R_{25} and R_{26} are, independently, -OH, -H, or $-NH_2$, and n=1 through 4.--

--27. (Amended) A method for treating an angiogenesis dependent disease in a human or animal having such a disease comprising administering to the human or animal a composition comprising an angiogenesis inhibiting compound and an antiinflammatory compound, wherein the angiogenesis inhibiting compound is selected from [the group consisting of]:

(1) a compound selected from the formula

A)



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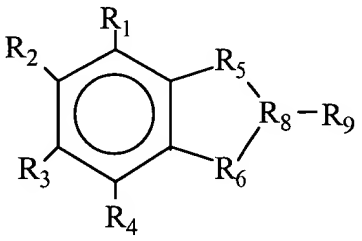
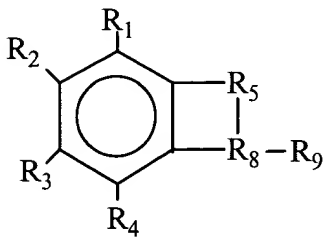


or

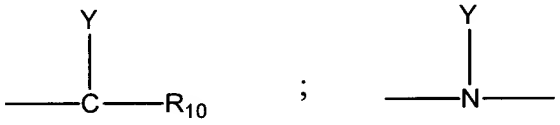
C)



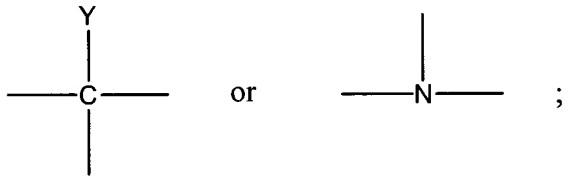
wherein

R_1 - R_4 are each independently selected from -H; -OH; =O; straight or branched chain alkanes, alkenes, and alkynes; cyclic alkanes, alkenes, and alkynes; combinations of cyclic and acyclic alkanes, alkenes, and alkynes; alcohol, aldehyde, ketone, carboxylic acid, ester, or ether moieties in combination with acyclic, cyclic, or combination acyclic/cyclic moieties; aza; amino; $-XO_n$ or $-O-XO_n$, where X=N and n=2, X=S and n=2 or 3, or X=P and n=1-3; and halogens;

$R_5 - [R_8]R_7$ are each independently selected from



or -O-, where Y is absent and R_{10} is =O or Y and R_{10} are each independently the same as R_1; where R_8 is independently selected from:



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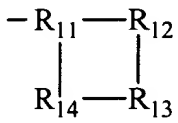
and R_9 is a moiety selected from [the group consisting of]

D)



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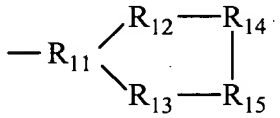

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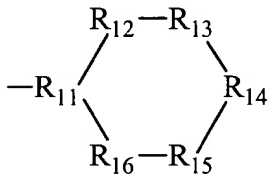
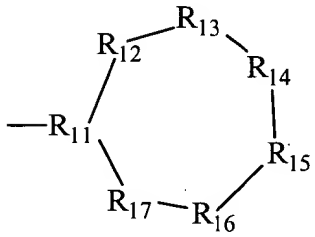
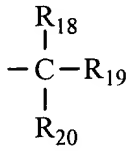


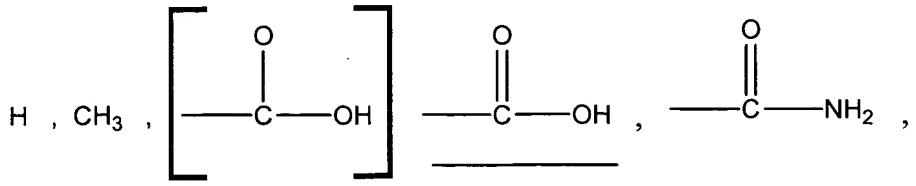
G)

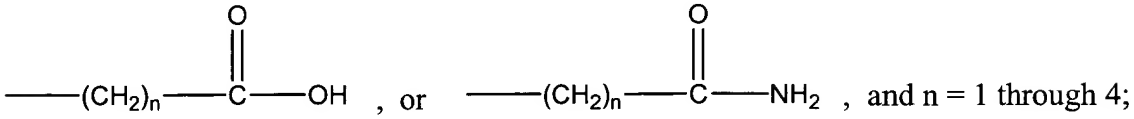


[and]or H)



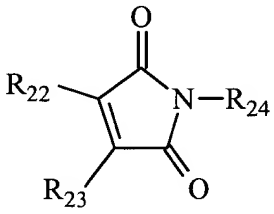
wherein each of [R_{11}] R_{12} - R_{17} is independently the same as R_5, wherein R_{11} is independently the same as R_8; and wherein R_{18}, R_{19} and R_{20} are each independently selected from





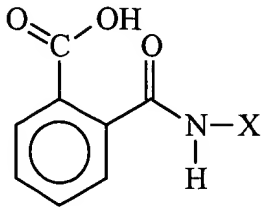
with the proviso that the angiogenesis inhibitory compound is not thalidomide;

(2) a compound selected from the formula

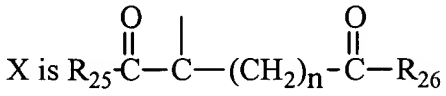


where R_{22} and R_{23} are each independently H, F, C_l, Br, I, CH_3, or $-CH_2-CH_3$;
and R_{24} is H, CH_3, or $-CH_2-CH_3$;
and

(3) a compound selected from the formula



where X is R_6 as defined in (1) above or



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and R_{25} and R_{26} are, independently, -OH, -H, or $-NH_2$, and n=1 through 4.--

--28. (Amended) The method of Claim 27 wherein the angiogenesis dependent disease is selected from macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasias, proliferative vitreoretinopathy, solid tumors, blood-borne tumors, leukemia, hemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy of prematurity, corneal graft rejection, epidemic keratoconjunctivitis, Vitamin A deficiency, contact lens overwear, atopic keratitis, superior limbic keratitis, pterygium keratitis sicca, sjogren's syndrome, acne rosacea, phylectenulosis, syphilis, *Mycobacteria* infections, lipid degeneration, chemical burns, bacterial ulcers, fungal ulcers, *Herpes simplex* infections, *Herpes zoster* infections, Mooren's ulcer, Terrien's marginal degeneration, marginal keratolysis, trauma, rheumatoid arthritis systemic lupus, polyarteritis, Wegener's sarcoidosis, scleritis, Stevens-Johnson disease, radial keratotomy, corneal graft rejection, sickle cell anemia, pseudoxanthoma elasticum, pemphigoid, Paget's disease, vein occlusion, artery occlusion, carotid obstructive disease, chronic uveitis, chronic vitritis, Lyme's disease, systemic lupus erythematosis, Eales' disease, Behcet's disease, presumed ocular histoplasmosis, Best's disease, myopia, optic pits, Stargardt's disease, pars planitis, chronic retinal detachment, hyperviscosity syndromes, toxoplasmosis, post-laser complications, [and]or rubeosis.--

--44. (Amended) The angiogenesis inhibitory composition of Claim 43 wherein the NSAID is [selected from] aspirin, acetominophen, ibuprofen, esculetin, phenidone, quercetin, ketoprofen, nordihydroguiaretic acid (NDGA), sulindac, sulindac sulfone, sulindac sulfide, indomethacin, NS-398 (a cyclooxygenase-2 inhibitor), cyclooxygenase-1 inhibitors, methylheptyl imidazole, furegrelate sodium, SKF525AHCL, thromboxane inhibitors, toradol, ecasa, salsalate, diflunisal, mefenamic acid, naproxen, naproxen sodium, floctafenine, meclofenamate, phenylbutazone, oxyphenbutazone, diclofenac, etodolac, fenoprofen, flufenamic acid, flurbiprofen, pirprofen, tolmetin, apazone, fenbufen, nabumetone, oxaprozin, piroxicam, salicylate, [and]or tenoxicam.--